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Can Robot Worms Kill Cancer?

Scientists Experiment With Microscopic Mechanical Worms to Find, Kill Cancer

By LEE DYE

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Scientists are creating tiny mechanical "nanoworms" that could zip through the human body like cruise missiles, finding cancerous tumors that are too small to be seen any other way.

That could lead to very early detection before the cancer even begins to spread, and ultimately these tiny vehicles 3 million times smaller than an earthworm may be able to deliver a lethal blow to the tumor.

"We want them to be able to release a drug and kill the tumor" without damaging adjacent tissue, said Michael Sailor, professor of chemistry and biochemistry at the University of California San Diego, who headed the research team. The team included scientists at UC Santa Barbara and the Massachusetts Institute of Technology who brought special skills to the project, which was revealed in a recent issue of the journal Advanced Materials.

The work is a significant advance in a hot-button field that is the cornerstone of many research projects around the world.

Scientists and engineers hope to create many incredibly small machines, such as nanoworms (so named because they are multi-jointed like earth worms) that can venture just about anywhere, including inside the human body. They will be designed for specific tasks, like the delivery of drugs to diseased organs, and then self-destruct and exit the body once their job has been completed.

The trick has been to come up with a design that allows the machines to escape the body's natural defense mechanisms and hang around long enough to get the job done, but not stay too long.

"Your body has all sorts of mechanisms to remove small molecules, big molecules, and even nano-particles or particulates like blood clots and anything that's not supposed to be there," Sailor said in an interview. That's obviously a good thing.

But organisms ranging from humans to lab rats are so good at ejecting toxic substances that it has been hard for scientists to come up with a material and a design that would fool the body's protective mechanisms long enough to get the job done.

"It's kind of a delicate balance," Sailor said. "You want it to stay long enough to find the tumors and do the damage, but once it's done its job, you want it to leave."

Sailor said the team achieved two "breakthroughs," a word that is not used lightly by scientists.

The researchers found that nanoworms coated with "sort of a slime" could escape the defense mechanisms in laboratory mice for up to 24 hours, long enough to find any potential tumors. And because of the design of the nanoworms, when they did link up with a tumor, they stood out brilliantly during body scans, making it much easier to zero in on the tumor.

The researchers used tiny balls of iron oxide, a material that increases contrast in magnetic resonance imaging scans. They were able to show, in a Petri dish, that the balls quickly attached to a tumor, apparently because blood vessels in tumors are quite leaky. Thus a lot of blood flows through the tumor, and some materials in the blood stream, like iron oxide balls, "just go in there and stick," sort of like a fish in a fish net, Sailor said.

It worked in a Petri dish, but when they tried it in mice, the protective mechanisms recognized the balls as intruders and kicked them out.

And then, partly by accident, team member Ji-Ho Park, a graduate student at UC San Diego, made an important discovery. He found that if he created a structure composed of several smaller iron oxide balls strung together like an earth worm and coated with what Sailor called "slime," it remained in the mice for up to 24 hours. It is not clear yet why that worked.

In addition, the researchers found that the nanoworms showed up in scans much more brilliantly than the balls if they were separated. In other words, the whole was brighter than the sum of its parts, suggesting it will be possible to see even much smaller tumors.

The "slime" that played such a critical role in this project really wasn't slime at all. It was actually a polymer coating with a tumor-targeting molecule, a peptide called F3, developed in the laboratory of Erkki Ruoslahti, a cell biologist at UC Santa Barbara and a member of the team. Because of the nanoworm's shape, many F3 molecules can be attached to it, thus increasing its ability to find tumors.

"We put a little fishing lure on these guys so they'll hook specifically onto the tumors," Sailor said.

That should make it possible for scientists to create nanoworms that will deliver drugs directly to tumors without killing nearby healthy cells, according to Sangeeta Bhatia of MIT, a physician who was part of the team.

That would give them a one-two punch find the tumor and kill it.

And then, as Sailor emphasized, get the heck out.

"Our mantra is it has got to be non toxic, and it has to be brief, and it has to degrade into nontoxic products as well," he said. "In the end, you want everything to leave the body."

But this is scientific research, not a cure for cancer. It will take many years, and much refinement, for this kind of research to move from the lab to the medical ward.

Lee Dye is a former science writer for the Los Angeles Times. He now lives in Juneau, Alaska.